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Cerebral oxygenation changes in the prefrontal cortex: Effects of age and gender

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Abstract

Multi-channel near-infrared spectroscopy (NIRS) is an optical method, which allows non-invasive in vivo measurements of changes in the concentration of oxygenated (O_2Hb) and deoxygenated (HHb) hemoglobin in living brain tissue, simultaneously from multiple measurement points. In the present study, 44 young and 42 elderly subjects were investigated by means of multi-channel NIRS (optical topography) during performance of the verbal fluency task (VFT). The aim of the study was to analyze the effects of the subjects' age and gender on functional brain activation during this cognitive task.

In summary, the results clearly show that the VFT activated the left and right dorsolateral prefrontal cortex (increases in O_2Hb and more localized decreases in HHb), with an obvious left-hemispheric dominance. The elderly subjects generally exhibited less activation and no left hemispheric lateralization effect. In contrast to a previous study, we did not find a clear influence of the subjects' gender on the brain activation pattern.

Keywords: Near-infrared spectroscopy; NIRS; Sex; Aging; Verbal fluency task

1. Introduction

Near-infrared spectroscopy (NIRS) has gained much attention in recent years as a methodology for functional neuroimaging. NIRS is based on the fact that unlike visible light near-infrared light (wavelength from 700 to 1000 nm) easily passes through biological tissues and is mainly absorbed by few chromophores like hemoglobin with different absorption spectra for their oxygenation–deoxygenation states. Regional brain activation leads to an increased oxygen metabolic rate and to an initial deoxygenation of the tissue which is followed by increased regional cerebral blood flow (rCBF). As this increased rCBF exceeds the initial deoxygenation of the tissue [13] brain activation normally leads to increased concentrations of O_2Hb and to decreased concentrations of HHb (for a more detailed description of the basics of NIRS see: [23,37,38,46]. Over the past years a number of functional brain activations studies have been published using NIRS during cognitive [10,11,16,18,19,36,42] and emotional tasks [15]. NIRS is a noninvasive technique, with low running costs, a high portability and the possibility for examinations in a natural setting. These advantages of the NIRS methodology makes it perfectly suitable to measure functional brain activity in psychiatric patients [9,12,17,32,33,44,47].

For the interpretation of the data it is very important to include demographic variables such as sex or age. Although gender differences in brain activation have been described for verbal tasks [41,49], a recent meta-analysis [45] did not reveal any general differences between males and females in language lateralization but only in some, not specified language tasks. In a recent NIRS study [26], no lateralization

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effects were described, but generally higher [O_2Hb] during a VFT for males as compared to females. The authors explained the missing lateralization with an active baseline condition, in which the subjects had to pronounce syllables. In contrast to this interpretation, a recent study [18] described higher increases over left prefrontal but not right prefrontal brain areas during the letter version of the VFT as compared to an active pronouncing task.

The effect of aging has repeatedly been associated with an age-dependent decline of brain activation during cognitive tasks as assessed by NIRS [22,29,34,43]. Many studies using other functional imaging methods such as fMRI and PET confirm these findings (e.g. [8,24,25]). An even more consistent result of such studies is a reduced lateralization, particularly within frontal brain areas, in older as compared to younger subjects ("Hemispheric Asymmetry Reduction in Old Adults", "HAROLD" model, e.g. [1–3,35,40]). In accordance with the existing literature, a previous NIRS study [26] found that young subjects had significantly higher increases in [O_2Hb] as compared to the elderly subjects during the VFT. Interestingly, the authors described significant interaction effects between sex and age, but did not explain in more detail the nature of these effects.

An influence of the factor age on the performance during tasks of word fluency has often been described in the past, even though many of these studies indicate a specific deficit in elderly subjects in semantic but not letter fluency (e.g. [31,39,48]), and results are still unclear as to whether the subjects' gender interacts with these age effects [7]. In any case, when using neuropsychological tests such as the VFT to investigate particular groups of subjects (e.g. psychiatric patients), it is essential to consider the influence of demographic variables such as the subjects' age and gender on associated cerebral activation patterns before drawing conclusions about the functioning of particular brain structures. Performance of the VFT has been suggested to involve Broca's area and prefrontal brain structures such as the dorsolateral prefrontal cortex (DLPFC) [4,6,14]. Since the DLPFC is a structure involved in many executive functions as well as psychopathological conditions, it is an interesting brain region well worth assessing in many neuro-psychiatric disorders, which makes the VFT particularly suited for the investigation of different clinical groups. However, without precise knowledge about the influence of demographic variables on this brain structure, interpretation of clinical data remains difficult.

Therefore, the aim of the present study was to investigate the effects of age and sex, and, most importantly, the interaction effect of sex and age on the functional hemodynamic response during a verbal fluency task. In expansion of the previous study [26], we investigated elderly instead of middle-aged subjects during two versions of the VFT, a letter and a category version. The analyses will focus on the effect of aging and sex on the activation pattern of the left and right dorsolateral prefrontal cortex measured with multi-channel NIRS.

2. Materials and methods

2.1. Subjects

In this study 44 young and 42 elderly subjects were investigated after written informed consent. In the young sample 22 men (mean age = 23.8 ± 2.6 years, range 19–31 years) and 22 women (mean age = 23.6 ± 1.6 years, range 22–28 years; no significant differences: $t[42] = 0.4$; $p = 0.73$), in the elderly sample 22 men (mean age = 5.3 ± 8.1 years; range 52–80 years) and 20 women (mean age = 62.7 ± 4.6 years, range 54–70 years; no significant differences: $t[33.9] = 1.3$; $p = 0.20$) were investigated. All subjects were right-handed and without actual or former psychiatric or neurological disease. In the elderly sample one subject smoked, 14 subjects were medicated for hypertension and two subjects were medicated for thyroid gland dysfunction.

2.2. Activation task

We used a block design with three 60-s blocks consisting of 30 s activation and 30 s resting period. Two different tasks were measured in alternating, balanced sequence over the subjects. The tasks were the verbal fluency task (VFT) in a letter and a category version. In the letter version of the VFT the participants were instructed to pronounce as many nouns as possible beginning with the letters "A", "F", and "S". Each of these three conditions (different starting letters) lasted 30 s. The correct verbal responses of the subjects were recorded by the investigators and used as a measure of behavioral performance. In the category version, the subjects were instructed to produce nouns belonging to the categories animals, fruits, and flowers. Before starting the measurements the subjects were instructed for the following task, told to close their eyes and to avoid movements.

2.3. Data measurement and processing

Relative changes in [O_2Hb] and [HHb] were measured with a 24-channel NIRS equipment (ETG-100 Optical Topography System; Hitachi Medical Co., Japan). The ETG-100 uses near infrared light at two wavelengths ranging around 787 and 827 nm (ranges: 782–793 and 823–833 nm). In this study, we used two arrays of 3 × 3 photodiodes (light detectors) and emitters (distance is 3 cm between the probes), which allowed us to measure the relative concentrations of hemoglobin at 12 measuring points in two areas of 6 cm × 6 cm. The probes were mounted on two plastic helmets that were held by adjustable straps over the subject's bilateral temporal prefrontal cortex (see Fig. 1). We used the electrode positions T3 (left) and T4 (right), respectively, according to the international 10–20 EEG system for reliably positioning the posterior and inferior edge of the NIRS probe. According to a recent study [20], this position corresponds to the superior temporal gyrus, Brodmann area 22 and 42. As can be seen in Fig. 1, the NIRS probe was